

2/7/4 (Item 4 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0014366584 BIOSIS NO.: 200300324880  
REGIONAL ANALYSIS OF GENE EXPRESSION IN THE EMBRYONIC MOUSE CORTEX.  
AUTHOR: Kudo L C (Reprint); Karsten S L; Levitt P; Geschwind D H  
AUTHOR ADDRESS: Neuroscience IDP, Neurology, UCLA, Los Angeles, CA, USA\*\*  
USA  
JOURNAL: Society for Neuroscience Abstract Viewer and Itinerary Planner  
2002 pAbstract No. 626.1 2002 2002  
MEDIUM: cd-rom  
CONFERENCE/MEETING: 32nd Annual Meeting of the Society for Neuroscience  
Orlando, Florida, USA November 02-07, 2002; 20021102  
SPONSOR: Society for Neuroscience  
DOCUMENT TYPE: Meeting; Meeting Poster; Meeting Abstract  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Determination of the temporal patterns of gene expression during brain formation has direct implications for the range of potential functions of that gene. In the context of the developing cerebral cortex, it has been suggested that the early parcellation of regions at the molecular level may underlie the subsequent formation of functional circuitry. In order to identify differential expression patterns of genes in various regions of the developing cerebral cortex, total RNA was isolated from three separate regions of mouse cerebral wall at E12.5, just after the onset of neuronogenesis. Transcripts were analyzed using a 9,500-element custom cDNA microarray. Four independent pools from each of these three regions, the future frontal, parietal, or occipital (F, P, O) regions of the mouse cerebral cortex, were compared (F vs. P, F vs. O) in duplicate for a total of 16 array hybridizations. Probe synthesis and hybridizations were performed using the tyramide signal amplification (TSA) protocol (NEN). Linear normalization and confidence analyzer (\*\*GeneSight\*\* 3.0, Biodiscovery) applied to the microarray data have revealed differentially expressed genes among the three regions, representing various functional categories related to transcriptional regulation, signal transduction, metabolic pathways, as well as ESTs. Several genes showed a gradient in the expression levels among the investigated regions. Spatial patterns of expression of these transcripts were assessed by in situ hybridization. Developmental patterns of identified genes will be used to make inferences as to their potential relevance for CNS development.

2/7/6 (Item 6 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0014196235 BIOSIS NO.: 200300154954  
Gene Expression Profiling In Human Age-related Macular Degeneration.  
AUTHOR: Brown D J (Reprint); Atilano S R (Reprint); Kenney M C (Reprint)  
AUTHOR ADDRESS: Ophthalmology Research Laboratories, Cedars-Sinai Medical Center, Los Angeles, CA, USA\*\*USA  
JOURNAL: ARVO Annual Meeting Abstract Search and Program Planner 2002 p Abstract No. 2834 2002 2002  
MEDIUM: cd-rom  
CONFERENCE/MEETING: Annual Meeting of the Association For Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA May 05-10, 2002; 20020505  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Purpose: To assess alterations in retinal and pigmented epithelium (RPE) gene expression that accompany age related macular degeneration (AMD) in human patients. Methods: Retinal and RPE tissues were obtained from autopsy material of patients with documented histories (including fundus photos) of AMD (n=8). Age and sex matched control tissues were obtained through the National Disease Research Interchange. Total RNA was isolated by extraction using Trizol (Invitrogen) and Poly A+ RNA isolated from the total RNA by magnetic bead separation. RNA quality and quantity were evaluated using an Agilent Bioanalyzer. Samples were then processed using the Smart cDNA protocol and the resulting cDNA was labeled with 32P-dATP. This material was then hybridized to cDNA arrays containing 3600 unique elements. Images were obtained using a Molecular Dynamics phosphorimager and stored as 16 bit TIF files. These files were evaluated using the Image processing software (BioDiscovery) and the results analyzed using \*\*\*GeneSight\*\*\* software (BioDiscovery). Results: The RNA obtained from these postmortem human tissues was of a consistent quality and quantity to utilize as a source for array based expression profiling. Smart cDNA synthesis was found to be highly reproducible and gave results similar to those obtained by direct RNA labeling methods. In this survey of 3600 genes, several hundred genes were identified with a 99% confidence level as either over or under expressed in AMD. Conclusion: Human postmortem tissue contains sufficient levels and quality of RNA to reliably perform array based analyses for gene expression profiling. Our results suggest that AMD retinal and RPE tissues have a variety of changes that generally cluster into functional groups encompassing alterations in extracellular matrix, cytokine profile, plasma membrane receptors and cell cycle regulators.

2/7/7 (Item 1 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
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09701894 Genuine Article#: 438KA Number of References: 2  
Title: Gene expression-based tumor classification with **GeneSight** (TM)  
from BioDiscovery, Inc.  
Author(s): ANONYMOUS  
Journal: CANCER RESEARCH, 2001, V61, N11 (JUN 1), PU3-U3  
ISSN: 0008-5472 Publication date: 20010601  
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202  
USA  
Language: English Document Type: ARTICLE  
Abstract: The most important aspect of expression microarray research is the interpretation of the massive amounts of raw data that array expression experiments generate. BioDiscovery's \*\*\*GeneSight\*\*\* helps you organize, prepare, and statistically analyze array data more quickly and easily than ever before. This system allows you to identify and compare differentially expressed genes with high statistical confidence.

2/7/8 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
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12001644 EMBASE No: 2003112993  
Gene expression in cancer: The application of microarrays  
Macgregor P.F.  
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Expert Review of Molecular Diagnostics ( EXPERT REV. MOL. DIAGN. ) (

United Kingdom) 2003, 3/2 (185-200)  
CODEN: ERMDC ISSN: 1473-7159  
DOCUMENT TYPE: Journal ; Review  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 80

Genome-wide monitoring of gene expression using DNA microarrays represents one of the latest breakthroughs in experimental molecular biology and provides unprecedented opportunity to explore the biological processes underlying human diseases by providing a comprehensive survey of a cell's transcriptional landscape. In the cancer field, this revolutionary technology allows the simultaneous assessment of the transcription of tens of thousands of genes, and of their relative expression between normal cells and malignant cells. As microarray analysis emerges from its infancy, there is widespread hope that microarrays will significantly impact on our ability to explore the genetic changes associated with cancer etiology and development, and ultimately lead to the discovery of new biomarkers for disease diagnosis and prognosis prediction, and of new therapeutic tools. This review provides an overview of microarray technology, specifically in the context of cancer research and describes some of its recent applications to the study of cancer. In addition, the challenges of translating microarray findings into molecular cancer diagnosis and prognosis tools, with the potential of altering clinical practice through individualized cancer care and ultimately of contributing to the battle against cancer, are discussed.

2/7/9 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
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11839682 EMBASE No: 2002412874  
Yellow pages to the transcriptome  
Scheel J.; von Brevern M.-C.; Horlein A.; Fischer A.; Schneider A.; Bach A.  
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AUTHOR EMAIL: scheel@axaron.com  
Pharmacogenomics ( PHARMACOGENOMICS ) (United Kingdom) 2002, 3/6 (791-807)  
CODEN: PARMF ISSN: 1462-2416  
DOCUMENT TYPE: Journal ; Review  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 100

Transcriptomics has become an important tool for the large-scale analysis of biological processes. This review aims to provide sufficient criteria to make an appropriate choice among the variety of 'closed' systems, represented by DNA microarrays, and 'open' systems like fragment display, tag sequencing and subtractive hybridization, depending on the biological system under investigation. The most important technologies currently available are presented, their strengths and weaknesses are discussed and companies active in the field are listed. The potential of transcriptomics in the pharmaceutical research and development process is highlighted by applications in oncology, research on neurological diseases, and predictive toxicology. Finally, a prognosis for future developments of the technologies is given.

2/7/10 (Item 3 from file: 73)  
DIALOG(R)File 73:EMBASE  
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11619893 EMBASE No: 2002192036

Analyzing array data using supervised methods

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Pharmacogenomics ( PHARMACOGENOMICS ) (United Kingdom) 2002, 3/3  
(403-415)

CODEN: PARMF ISSN: 1462-2416

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 55

Pharmacogenomics is the application of genomic technologies to drug discovery and development, as well as for the elucidation of the mechanisms of drug action on cells and organisms. DNA microarrays measure genome-wide gene expression patterns and are an important tool for pharmacogenomic applications, such as the identification of molecular targets for drugs, toxicological studies and molecular diagnostics. Genome-wide investigations generate vast amounts of data and there is a need for computational methods to manage and analyze this information. Recently, several supervised methods, in which other information is utilized together with gene expression data, have been used to characterize genes and samples. The choice of analysis methods will influence the results and their interpretation, therefore it is important to be familiar with each method, its scope and limitations. Here, methods with special reference to applications for pharmacogenomics are reviewed.

2/7/11 (Item 1 from file: 315)

DIALOG(R) File 315:ChemEng & Biotec Abs

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492805 CEABA Accession Number: 33-07-005261 DOCUMENT TYPE: Journal

Title: Query tools for microarray data mining applications

AUTHOR: Groch, K. ; Kuklin, A.

CORPORATE SOURCE: BioDiscovery Inc, Marina Del Rey, California, USA

JOURNAL: LC GC Europ., Volume: 14, Issue: 8 Proteomics & Drug Development

, Page(s): 54-56

ISSN: 08955441

PUBLICATION DATE: 2001 (20010000)

ABSTRACT: Microarray experiments generate an enormous amount of numerical data making their maintenance and analysis difficult. Integrating additional information like gene annotations to the microarray data to understand the functional relationships between genes is another challenge faced while handling and analyzing the microarray data. The software, **GeneSight**, is a user friendly and convenient solution to this problem addressing both numerical and text-based needs. It contains two tools, Template Matcher and Query/Group Builder to query data set and integrate textual information respectively. **GeneSight** has many important features and advantages useful in fishing out the gene(s) from the database on the basis of expression pattern and relating it to its biological functions. This article elaborates on the DNA microarrays and gene expression studies carried out in *Saccharomyces cerevisiae* using this software.

2/7/12 (Item 1 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

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136032293 CA: 136(3)32293r JOURNAL

Gene expression pattern analysis with clustering in the data mining  
system GeneSight

AUTHOR(S): Hoff, Bruce; Kuklin, Alexander; Shams, Soheil  
LOCATION: BioDiscovery Inc., Los Angeles, CA, 90064, USA  
JOURNAL: Bioforum Int. (Bioforum International) DATE: 2001 VOLUME: 5  
NUMBER: 1 PAGES: 25-26,28 CODEN: BINTFQ ISSN: 1434-2693 LANGUAGE:  
English PUBLISHER: GIT Verlag GmbH

SECTION:

CA203001 Biochemical Genetics

IDENTIFIERS: gene expression clustering data mining system GeneSight

DESCRIPTORS:

Gene...

expression; gene expression pattern anal. with clustering in data  
mining system GeneSight

Cluster analysis... Bioinformatics... Algorithm...

gene expression pattern anal. with clustering in data mining system  
GeneSight

2/7/13 (Item 1 from file: 9)  
DIALOG(R) File 9:Business & Industry(R)  
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2788496 Supplier Number: 02788496 (THIS IS THE FULLTEXT)  
Internet Broadens the Availability of Bioinformatics Tools  
(Bioinformatics market is projected to grow to \$1.5-2 bil over next five  
years; Internet is becoming more important to bioinformatic vendors)  
Chemical Market Reporter, v 257, n 17, p 22  
April 24, 2000  
WORD COUNT: 682

TEXT:

BY CYNTHIA CHALLENGER

THE INTERNET is becoming important part for bioinformatic vendors.

About 50 companies are selling bioinformatics products. Most of them are  
privately held, making it difficult to determine the size of the market.  
Industry estimates place the market at roughly \$300 million, according to  
Front Line Management Consulting Inc. and Frost and Sullivan.

The bioinformatics market is expected to grow to \$1.5 billion to \$2 billion  
over the next five years, with top-line growth of 25 to 35 percent. If  
internal company spending on bioinformatics IT is included, the overall  
market may exceed the \$2 billion mark during this period, notes Jason Reed,  
biotechnology analyst for Oscar Gruss. These numbers do not include R&D  
collaborations between pharma, agbio and genomics companies that involve  
bioinformatics content.

Leading bioinformatics vendors include BioDiscovery (product:  
**GeneSight**), GeneData (product: Expressionist), GeneLogic (product:  
GeneExpress), Silicon Genetics (product: GeneSpring), DoubleTwist Inc.  
(product: DoubleTwist.com), eBioinformatics (product: BioNavigator.com).

Several key features drive the success of bioinformatics tools. "Users want  
customized data accessibility through open architecture, standardization of  
data formats, and multi-format data management tools," says Robert Cohen, a  
consultant for Front Line Management Consulting.

Specifically, bioinformatics is used to search for regions of homology  
(match) between sequences of DNA or proteins, to identify lead compounds  
(potential drugs) for high-throughput screening studies, to analyze gene  
expression data from microarrays (DNA chips), and for mining protein  
databases to understand three-dimensional structures.

"There are several developments that have affected and will continue to

affect the use of bioinformatics tools," Mr. Cohen says. He cites the completion of the human genome sequence by Celera, announced earlier this month, and the need to compare information across genomes for different models (mouse versus human, for example) as a key area.

Other areas of importance include the trend toward proteomics (protein analysis) and eventually metomics (metabolic pathway analysis), and the increased use of microarray technology.

The latest major development is the use of the Internet as a means of providing access to bioinformatics technology to individual researchers and organizations that cannot afford to purchase the necessary hardware and software for in-house use.

Although genomic information is widely available on the Internet (one source is the Canadian Bioinformatics Resource: [www.cbr.nrc.ca](http://www.cbr.nrc.ca)), it has only been in the last two years that commercial suppliers of bioinformatics tools have moved onto the Web.

Two such ventures are eBioinformatics Inc. (Pleasanton, Calif.) and DoubleTwist Inc. (Oakland, Calif.--formerly Pangea Systems). Both BioNavigator and DoubleTwist.com are application service provider (ASP) models that allow access to bioinformatics tools and information via the Web.

Those companies say that the key to the success of bioinformatics companies will be their ability to provide easy-to-use tools that are available for use by individual scientists and researchers.

"The restricted availability comes in several forms--cost of the good programs, the difficulty of using several different tools when each has its own unique interface, the special and expensive computer hardware required to run the programs, and the training the biologist needs to understand the use of the rather broad assortment of differing bioinformatics software," explains James Nelson, vice-president of product marketing for eBioinformatics.

John Couch, president and CEO of DoubleTwist, notes that the Internet has provided a means for DoubleTwist to extend its market reach from primarily large pharmaceutical companies to the individual life scientist.

Both DoubleTwist and eBioinformatics are banking on the ASP model. "Users will no longer have to, or want to, purchase expensive software nor the hardware required to run it," Mr. Nelson says. "Instead, users will simply rent the time the way they now rent long-distance phone service. Independent software vendors will be forced to adopt the Internet as their main method of product delivery rather than selling directly to the end user." Mr. Couch also confirms that DoubleTwist sees a shift away from enterprise software to the ASP model.

The infrastructure of the Internet is currently the main factor limiting the kinds of programs that can be placed into the ASP model, adds Mr. Nelson. As new broadband Internet backbones come on line, it will become possible to put any program into the ASP model.

16025079 PMID: 12874046

Noise sampling method: an ANOVA approach allowing robust selection of differentially regulated genes measured by DNA microarrays.

Draghici Sorin; Kulaeva Olga; Hoff Bruce; Petrov Anton; Shams Soheil; Tainsky Michael A

Department of Computer Science, Wayne State University, 431 State Hall, Detroit, MI, 48202, USA. sod@cs.wayne.edu

Bioinformatics (Oxford, England) (England) Jul 22 2003, 19 (11) p1348-59, ISSN 1367-4803 Journal Code: 9808944

Contract/Grant No.: P30CA022453; CA; NCI

Document type: Evaluation Studies; Journal Article; Validation Studies

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

MOTIVATION: A crucial step in microarray data analysis is the selection of subsets of interesting genes from the initial set of genes. In many cases, especially when comparing a specific condition to a reference, the genes of interest are those which are differentially expressed. Two common methods for gene selection are: (a) selection by fold difference (at least  $n$  fold variation) and (b) selection by altered ratio (at least  $n$  standard deviations away from the mean ratio). RESULTS: The novel method proposed here is based on ANOVA and uses replicate spots to estimate an empirical distribution of the noise. The measured intensity range is divided in a number of intervals. A noise distribution is constructed for each such interval. Bootstrapping is used to map the desired confidence levels from the noise distribution corresponding to a given interval to the measured log ratios in that interval. If the method is applied on individual arrays having replicate spots, the method can calculate an overall width of the noise distribution which can be used as an indicator of the array quality. We compared this method with the fold change and unusual ratio method. We also discuss the relationship with an ANOVA model proposed by Churchill et al. In silico experiments were performed while controlling the degree of regulation as well as the amount of noise. Such experiments show the performance of the classical methods can be very unsatisfactory. We also compared the results of the 2-fold method with the results of the noise sampling method using pre and post immortalization cell lines derived from the MDAH041 fibroblasts hybridized on Affymetrix GeneChip arrays. The 2-fold method reported 198 genes as upregulated and 493 genes as downregulated. The noise sampling method reported 98 gene upregulated and 240 genes downregulated at the 99.99% confidence level. The methods agreed on 221 genes downregulated and 66 genes upregulated. Fourteen genes from the subset of genes reported by both methods were all confirmed by Q-RT-PCR. Alternative assays on various subsets of genes on which the two methods disagreed suggested that the noise sampling method is likely to provide fewer false positives.

Record Date Created: 20030722

Record Date Completed: 20040420

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2 (Item 2 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
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09230371 Genuine Article#: 382BJ Number of References: 16  
Title: Information processing issues and solutions associated with  
**microarray** technology  
Author(s): Kuklin A (REPRINT) ; Shah S; Hoff B; Shams S  
Corporate Source: BIODISCOVERY INC, 1150 W OLYMPIC BLVD, SUITE 1170/LOS  
ANGELES//CA/90064 (REPRINT)  
Journal: LABORATORY ROBOTICS AND AUTOMATION, 2000, V12, N6 (DEC), P317-327  
ISSN: 0895-7533 Publication date: 20001200  
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012  
Language: English Document Type: ARTICLE  
Abstract: Managing vast amounts of information associated with DNA array  
technology presents a challenge. This article describes a synergistic  
analysis management (SAM) system, which integrates **microarray** and  
laboratory data along with analysis steps to present a synergistic view  
to the researcher. We describe tools for data management in array  
fabrication, automated image analysis, and array data mining. All the  
described modules allow for seamless POW of information and are  
connected through a database. SAM will enhance \*\*\*microarray\*\*\*  
projects at pharmaceutical and academic institutions, which face the  
problems of high throughput \*\*\*microarray\*\*\* data management. (C) 2000  
John Wiley & Sons, Inc.

5/7/3 (Item 1 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)  
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11453751 PMID: 11560067  
Experimental design, analysis of variance and slide quality assessment in  
gene expression arrays.  
Draghici S; Kuklin A; Hoff B; Shams S  
BioDiscovery Inc, 11150 West Olympic Boulevard, Suite 1170, Los Angeles,  
CA 90064, USA. sorin@biodiscovery.com  
Current opinion in drug discovery & development (England) May 2001, 4  
(3) p332-7, ISSN 1367-6733 Journal Code: 100887519  
Document type: Journal Article; Review; Review, Tutorial  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed  
A **microarray** experiment is a sequence of complicated molecular  
biology procedures relying on various laboratory tools, instrumentation and  
experimenter's skills. This paper discusses statistical models for  
distinguishing small changes in gene expression from the noise in the  
system. It describes methods for assigning statistical confidence to gene  
expression values derived from a single array slide. Some of the theory is  
discussed in the context of practical applications via software usage. (10  
Refs.)  
Record Date Created: 20010918  
Record Date Completed: 20020219

5/7/5 (Item 2 from file: 357)  
DIALOG(R) File 357:Derwent Biotech Res.  
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0318614 DBR Accession No.: 2003-19754 PATENT  
**Microarray** data modification method for analyzing complex biochemical  
samples, involves applying user-selected, user- sequenced mathematical  
data preparation operations to **microarray** data - data sequence  
**microarray** analysis using bioinformatic software



AUTHOR: HOFF B; SHAMS S; DRAGHICI S; AOKI K  
PATENT ASSIGNEE: HOFF B; SHAMS S; DRAGHICI S; AOKI K 2003  
PATENT NUMBER: US 20030071843 PATENT DATE: 20030417 WPI ACCESSION NO.:  
2003-522296 (200349)  
PRIORITY APPLIC. NO.: US 981865 APPLIC. DATE: 20011017  
NATIONAL APPLIC. NO.: US 981865 APPLIC. DATE: 20011017  
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Several user-selectable, user-sequential mathematical data preparation operations (DPOs) (25-27) are displayed in a table format. The DPOs are varied by a user, using the transformations (21-23). The user selected DPOs that are dragged and dropped into an assembly area (24), are applied to the \*\*\*microarray\*\*\* data to produce modified data for storage. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a system for modifying **microarray** data; (2) computer readable medium storing **microarray** data modifying program; and (3) a method for normalizing \*\*\*microarray\*\*\* data. USE - For modifying **microarray** data obtained by performing experiment on known genetic materials such as nucleic acid, protein or small molecules cells for analyzing complex biochemical samples, using computer system. ADVANTAGE - Allows a user to control the order of the data preparation operations that are applied to data and provides useful interaction and feedback regarding the effects of the chosen numerical operations. (10 pages)

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